IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
TYLER DIVISION

MEDICAL RESEARCH INSTITUTE,	§	
	§	
Plaintiff,	§	
	§	
vs.	§	**CASE NO. 605 CV 417**
	§	**PATENT CASE**
BIO-ENGINEERED SUPPLEMENTS &	§	
NUTRITION, INC., et al.,	§	
	§	
Defendants.	§	

MEMORANDUM OPINION

This Claim Construction Opinion construes terms in U.S. Patent No. 6,905,707 B2 (filed Aug. 23, 2002)("the '707 patent").

BACKGROUND

Medical Research Institute ("MRI") alleges that Bio-Engineered Supplements & Nutrition, Inc. ("BSN") infringes the '707 patent. The '707 patent discloses a controlled release oral-dosage formulation for arginine α-ketoglutarate ("AAKG") and a method of treating atherosclerosis in a human patient by administering a controlled release formulation of AAKG.

AAKG is a known compound with known health benefits. However, prior art formulations of AAKG were quickly metabolized—limiting the potential health benefits—and could cause gastric discomfort in larger dosages. The '707 patent teaches a controlled release formulation of AAKG that is allegedly superior to a quick release formulation because it maintains a therapeutically effective blood serum level of AAKG for a longer period of time.

As originally submitted to the Patent and Trademark Office ("PTO"), the formulation of independent claim 1

> compris[ed]: a therapeutically effective amount of [AAKG]; and an excipient material; wherein the formulation is characterized by releasing the [AAKG] in a manner so as to increase a period of time over which a therapeutic level of [AAKG] is maintained as compared to a quick release formulation.

Independent claim 10 as originally submitted to the PTO was for a

> method of treating a human patient, comprising: administering to a human patient a controlled release formulation of [AAKG] which formulation is characterized by maintaining a therapeutic level of [AAKG] in the patient's circulatory system over a period of time greater than that obtained with a quick release formulation; and repeating the administering on three or more consecutive days thereby maintaining a therapeutic level of [AAKG] in the patient's circulatory system over a therapeutically effective period of time on three or more consecutive days.

The PTO Examiner did not reject these claims outright, but did suggest two changes to place the application in condition for allowance: (1) to incorporate the amounts of AAKG and excipient into claims 1 and 10 and (2) to incorporate a Markush group into claim 1 listing the specific controlled release excipients.

The claims were allowed after the patentee amended independent claims 1 and 10. The patentee amended claim 1 by (1) changing the amount of AAKG from "a therapeutically effective amount" to "about 50-70%," (2) changing "an excipient material" to "an excipient material comprising the remainder of the formulation," and (3) adding "wherein the excipient material is chosen from [a specific list of controlled release excipients] and mixture thereof." The patentee did not include a specific amount of AAKG in claim 10 and instead changed "a method of treating a human patient" to "a method of treating atherosclerosis in a human patient."

APPLICABLE LAW

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (quoting *Innova/Pure Water Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). In claim construction, courts examine the patent's intrinsic evidence to define the patented invention's scope. *See id.*; *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 861 (Fed. Cir. 2004); *Bell Atl. Network Servs., Inc. v. Covad Commc'ns Group, Inc.*, 262 F.3d 1258, 1267 (Fed. Cir. 2001). This intrinsic evidence includes the claims themselves, the specification, and the prosecution history. *See Phillips*, 415 F.3d at 1314; *C.R. Bard, Inc.*, 388 F.3d at 861. Courts give claim terms their ordinary and accustomed meaning as understood by one of ordinary skill in the art at the time of the invention in the context of the entire patent. *Phillips*, 415 F.3d at 1312–13; *Alloc, Inc. v. Int'l Trade Comm'n*, 342 F.3d 1361, 1368 (Fed. Cir. 2003).

The claims themselves provide substantial guidance in determining the meaning of particular claim terms. *Phillips*, 415 F.3d at 1314. First, a term's context in the asserted claim can be very instructive. *Id*. Other asserted or unasserted claims can also aid in determining the claim's meaning because claim terms are typically used consistently throughout the patent. *Id*. Differences among the claim terms can also assist in understanding a term's meaning. *Id*. For example, when a dependent claim adds a limitation to an independent claim, it is presumed that the independent claim does not include the limitation. *Id*. at 1314–15.

"[C]laims 'must be read in view of the specification, of which they are a part.'" *Id*. (quoting *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc)). "[T]he specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive;

it is the single best guide to the meaning of a disputed term.'" *Id*. (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1325 (Fed. Cir. 2002). This is true because a patentee may define his own terms, give a claim term a different meaning than the term would otherwise possess, or disclaim or disavow the claim scope. *Phillips*, 415 F.3d at 1316. In these situations, the patentee's lexicography governs. *Id*. Also, the specification may resolve ambiguous claim terms "where the ordinary and accustomed meaning of the words used in the claims lack sufficient clarity to permit the scope of the claim to be ascertained from the words alone." *Teleflex, Inc.*, 299 F.3d at 1325. But, "'[a]lthough the specification may aid the court in interpreting the meaning of disputed claim language, particular embodiments and examples appearing in the specification will not generally be read into the claims.'" *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) (quoting *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1571 (Fed. Cir. 1988)); *see also Phillips*, 415 F.3d at 1323. The prosecution history is another tool to supply the proper context for claim construction because a patent applicant may also define a term in prosecuting the patent. *Home Diagnostics, Inc., v. Lifescan, Inc.*, 381 F.3d 1352, 1356 (Fed. Cir. 2004) ("As in the case of the specification, a patent applicant may define a term in prosecuting a patent.").

Although extrinsic evidence can be useful, it is "'less significant than the intrinsic record in determining the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc.*, 388 F.3d at 862). Technical dictionaries and treatises may help a court understand the underlying technology and the manner in which one skilled in the art might use claim terms, but technical dictionaries and treatises may provide definitions that are too broad or may not be indicative of how the term is used in the patent. *Id*. at 1318. Similarly, expert testimony may aid

a court in understanding the underlying technology and determining the particular meaning of a term in the pertinent field, but an expert's conclusory, unsupported assertions as to a term's definition is entirely unhelpful to a court. *Id*. Generally, extrinsic evidence is "less reliable than the patent and its prosecution history in determining how to read claim terms." *Id*.

THE '707 PATENT[1]

Arginine α-ketoglutarate

The parties and the Court agree that the term should be construed according to the patent definition as

> arginine α-ketoglutarate which is a salt also known as arginine 2-ketoglutarate, arginine 2-oxoglutamate, and arginine 2-oxopentanedioic acid. Unless specified, the term covers racemic mixture as well as any other (non-50/50) mixture of the enantiomers including substantially pure forms of either the R-(+) or the S-(-) enantiomer. Further, unless specified otherwise the term covers pharmaceutically acceptable salts (e.g. Na and K salts) and amides, esters and metabolites of the acid.

'707 Patent col.4:40-49.

Excipient material

The parties and the Court agree that the term should be construed according to the patent definition as "any compound forming a part of the formulation which is intended to act merely as a carrier, i.e., not intended to have biological activity itself." '707 Patent col.4:66-67; 5:1-2.

About 50-70%

The Court agrees with MRI that this term does not require construction.[2] BSN argues that

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[1] Appendix A contains the patent claims with the disputed terms in bold.

[2] While the parties dispute—without detailed briefing—the level of ordinary skill in the art for the '707 patent, the Court's construction is not affected because the disputed terms are either defined in the patent or are ordinary words not specific to the art to be construed according to their customary meaning.

the term should be restricted at two significant digits (i.e. 49.5–70.5%) for two reasons: (1) 50 and 70 each have either one or two significant digits and (2) the specification stated a preferred range of 55–65% and these numbers have two significant digits. *See Athletic Alternatives, Inc. v. Prince Mfg., Inc.*, 73 F.3d 1573, 1581 (Fed Cir. 1996) (adopting the narrower construction of a term that had conflicting but equally plausible meanings). However, there are no contradictory interpretations of this term that would require a narrow interpretation. *See id.* Furthermore, BSN's proposed construction improperly imports a claim limitation from the specification. *See Phillips*, 415 F.3d at 1323.

An excipient material comprising the remainder of the formulation

The Court modifies BSN's proposed construction and construes the term as "the formulation includes only AAKG and excipient materials."

MRI argues that "comprising" is an open patent term and therefore "the formulation-in-question must include at least one excipient material from the list but does not exclude additional, unrecited elements." *See* U.S. PTO, Manual of Patent Examination Procedure ("MPEP") § 2111.03. MRI further contends that the use of "comprising" in both the preamble and in the term-at-issue shows the patentee's intent to leave the claim open to additional elements. MRI argues that the term is open because the Patent Examiner never outright rejected the original, open claim. However, MRI's construction improperly reads out the term limitations because there is no difference between its construction of "an excipient material comprising the remainder of the formulation" and the pre-amendment "an excipient material." The patentee added a limitation that must be given effect. *See Schoenhaus v. Genesco, Inc.*, 440 F.3d 1354, 1359 (Fed. Cir. 2006) (stating there must be a "substantial reason relating to patentability for including the limiting element added by

amendment").

BSN argues that the term is closed to additional elements for two reasons. First, while "comprising" is always construed as an open term when used in a claim preamble, it has no such automatic meaning when used within the body of a claim. *See Moleculon Research Corp. v. CBS, Inc*., 793 F.2d 1261, 1272 n.8 (Fed. Cir. 1986) (construing "comprising" according to normal rules of claim interpretation where the term was not used as part of a transitional phrase). The Court agrees with BSN that "comprising" in the body of the term should be construed according to normal claim construction rules.

Second, BSN argues that MRI acquiesced to a closed claim term during patent prosecution. *See Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 978-79 (Fed. Cir. 1999) ("Acquiescence may be found where the patentee narrows his or her claims by amendment . . . .") (citation omitted). The term "comprising" in the preamble of claim 1 is an open term, and as originally submitted the claim was open to additional elements. However, the Patent Examiner suggested that the patentee specify the amounts of AAKG and excipient in claim 1, and the patentee amended claim 1 to include "about 50-70% [AAKG]" and "an excipient material comprising the remainder of the formulation." The Court construes "remainder" according to its ordinary and customary meaning as "a quantity that remains after subtraction." *See* WEBSTER'S ENCYCLOPEDIA UNABRIDGED DICTIONARY OF THE ENGLISH LANGUAGE 1213 (1st ed. 1989); *Phillips*, 415 F.3d at 1312-13. The Court agrees with BSN that the patentee's amendment indicates that the excipient amount is defined as 100% of the formulation minus the AAKG. Therefore, because the patentee added the term-in-issue, claim 1 is an exception to the general rule that a claim using "comprising" in the preamble is open. This construction is consistent with all twenty-seven preferred embodiments, which contain only excipient

and AAKG. *See* '707 Patent col.8:18-10:50; *Phillips*, 415 F.3d at 1314-15.

Wherein the excipient is chosen from [a list of excipients][3], and mixture thereof

The Court agrees with MRI, modifies BSN's proposed construction, and construes the term as "wherein the excipient is chosen from [a list of excipients], and mixtures of two or more of the above listed excipients and may include excipients not listed." BSN argues that the formulation only includes excipients listed because the list is a closed Markush group. *See Abbott Labs v. Baxter Pharm. Prods., Inc*., 334 F.3d 1274, 1280 (Fed. Cir. 2003). BSN argues that the list is a closed Markush group because the Patent Examiner suggested an amendment to claim 1 to incorporate a Markush group of specific controlled release excipients.

BSN's argument is unconvincing. First, a Markush group must be "characterized with the transitional phrase 'consisting of,' rather than 'comprising' or 'including.'" *Id*. at 1280-81. MPEP section 2173.05(h) states that "it is improper to use the term 'comprising' instead of 'consisting of,' when drafting a Markush group." While the Patent Examiner did suggest incorporation of a controlled-release excipient Markush group, the patentee's claim 1 amendment lacked the language necessary to create a closed group. *See Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1372 (Fed. Cir. 2005) (holding that "group of" did not create a Markush group because "consisting" did not appear in the disputed claim).

Second, it is useful to clarify that patentee broadly defined excipient in the patent as any compound that is "intended to act merely as a carrier, i.e., not intended to have any biological

[3] "[A] list of excipients" substitutes for the controlled-release excipients listed in claim 1: "microcrystalline cellulose, hydroxypropylmethyl cellulose, ethylcellulose, cellulose acetate butyrate, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyethylene oxide, polyvinylpyrrolidone, polyethylene glycol, zein, poly-DL-lactide-co-glycolide, dicalcium phosphate, [and] calcium sulfate." '707 Patent col.19:40-47.

activity itself." '707 Patent col.4:66-5:2. Claim 1 as originally submitted did not identify controlled-release excipients and the Patent Examiner suggested the addition of a controlled-release excipient Markush group. The patentee's amendment—rather than add a Markush group—states that the excipient is chosen from a specified list of controlled-release excipients and "mixture thereof." The Court agrees with MRI that the formulation includes at least one listed controlled-release excipient, but does not exclude unlisted excipients because "mixture" refers to a combination of ingredients that includes at least one listed ingredient. *See Mars, Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1374-75 (Fed. Cir. 2004) (holding that "mixture" is an open-ended term).

Finally, BSN's construction is unduly restrictive because it excludes at least twenty of the twenty-seven preferred embodiments. *See, e.g., Glaxo Group Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 347 (Fed Cir. 2004) ("[C]laims should rarely, if ever, be construed to exclude a preferred embodiment."). MRI's interpretation encompasses the preferred embodiments, some of which use generic terms that would include species that became part of the claim language.[4]

Therapeutic level

The Court agrees with MRI and construes the term as "a level that is above the baseline level in the body and is sufficient to obtain the desired therapeutic result." BSN argues that the term should be construed as "at least 25 ng/mL of [AAKG] in the patient's circulatory system and in a sufficient level that is sufficient to treat the disease in the patient taking the formulation." BSN bases its argument on the specification, which states "a formulation of the invention releases active

[4] BSN alleges in its brief that MRI's interpretation excludes five of the preferred embodiments—embodiments 1-3 and 17-18. The Court is not persuaded that this is technically correct since some of the examples use generic terms—e.g. "organic polymer"—that would be understood to encompass claimed materials such as microcrystalline cellulose.

ingredient so as to obtain a blood serum level in a human patient in a range of about 25 to about 75 ng/mL of plasma." '707 Patent col.6:22-25.

BSN's argument fails because it seeks to import a claim limitation from the specification. *See Phillips*, 415 F.3d at 1323-28. BSN construes a specification example that states "a formulation of the invention" to mean "*every* formulation" or "the *only* formulation." There is no basis for this narrow construction.[5] *See id.*

The specification states that "therapeutic level" is a general term which varies for each patient because the amount needed "to obtain an optimum therapeutic[] effect will vary with a number of factors known to those skilled in the art, e.g., the size, age, weight, sex and condition of the patient." '707 Patent col.5:48-50. The specification also states that a formulation releases AAKG "so as to obtain a blood serum level in a human patient in a range of *about* 25 to 75 ng/mL of plasma." '707 Patent col.6:22-25 (emphasis added). In light of the specification's clear statements that the therapeutic level is variable and that *a* formulation results in a serum level of *about* 25 ng/mL, there is no basis requiring a blood serum level of at least 25 ng/mL AAKG. *See Phillips*, 415 F.3d at 1323-28.

Method of Treating Atherosclerosis

Because this term appears in the preamble of claim 10, the Court must first determine whether this term is limiting. The Court agrees with BSN that it is. The Patent Examiner suggested that the patentee include the amount of AAKG and excipient into claim 10 to place the application in condition for allowance. Instead, the patentee amended claim 10 by inserting "atherosclerosis in"

[5] If the Court were to adopt BSN's approach of importing limitations from specification examples, then the term would also have at least two other limitations. *See* '707 Patent col.5:47 (giving an example of daily dosage); '707 Patent col.6:37-42 (giving a preferred number of days to maintain the therapeutic level).

after the phrase "method of treating."

MRI argues that "atherosclerosis" is only a reference point such that *any* administration of the formulation sufficient to treat atherosclerosis is within the method, regardless of whether there is any intent to treat atherosclerosis. The Court rejects MRI's argument because it effectively reads "atherosclerosis" out of the claim contrary to the presumption that there is a "substantial reason relating to patentability for including the limiting element added by amendment." *Schoenhaus*, 440 F.3d at 1359; *see also Exxon Chem. Patents, Inc. v. Lubrizol Corp*., 64 F.3d 1553, 1557 (Fed. Cir. 1995)("[W]e must give meaning to all the words in [the] claim."). Therefore, the term limits claim 10 to a method that is intended to treat atherosclerosis.

The Court agrees with MRI and construes the term "treating" according to the '707 patent definition of "treatment" as

> obtaining a desired pharmacological and physiological effect. The effect may be prophylactic in terms of preventing or partially preventing a disease, symptom or condition thereof and/or may be therapeutic in terms of a partial or complete cure of a disease, condition, symptom or adverse effect attributed to the disease.

'707 Patent col.5:6-12; *see also Phillips*, 415 F.3d at 1316. BSN argues that "treating" in the term-at-issue is limited to treating an actual disease because the patentee distinguished between treating diseases from treating symptoms in the specification and therefore only claimed treatment as to a disease by using a disease term in the claim. This argument is unpersuasive because the '707 patent defines "treatment" of a disease to include preventative measures before any diagnosis is made. The specification examples of treating "symptoms" or "adverse effects" are just that, examples of treatments within the broad range of potential treatment. *See* '707 Patent col.7:44-47; col.5:8-11.

The Court construes atherosclerosis as "a disease, symptom, or condition characterized by

a progressive narrowing and hardening of the arteries." The patent does not define atherosclerosis, but extrinsic evidence supports the Court's construction. *See* WEBSTER'S NEW WORLD MED. DICTIONARY 29, 33 (2d ed. 2006); *Phillips*, 415 F.3d at 1318. BSN's proposed construction of atherosclerosis as "a disease, involving abnormal fatty deposits in a[] fibrosis of the inner lining of arteries" is too narrow. BSN relies on a dictionary definition that does not support its contention that fatty deposits are necessary; the definition states that "[a]therosclerosis is a multistage process set in motion when cells lining the arteries are damaged . . . high density lipoproteins accumulate at the site of arterial damage," making clear that fatty deposits occur *after* arterial linings are damaged. STEDMAN'S MED. DICTIONARY 162 (26th ed. 1995). Furthermore, BSN's interpretation includes terms that would also require construction (e.g., fatty deposits, fibrosis). To the extent that atherosclerosis involves accumulating arterial deposits, these symptoms are reflected in the Court's construction (i.e., "a progressive narrowing and hardening of the arteries").

Human patient

The Court construes the term as "a recipient of any various personal health services." MRI argues that "human patient" means "any person to whom the formulation-in-question has been, is, and/or will be administered." BSN argues that the term means "a human under medical care and treatment."

The intrinsic record does not support either proposed construction. The Court is not persuaded by MRI's argument that a person who elects to take the formulation is a "patient" simply because he administers the formulation to himself. The patentee included "patient" in the '707 patent without providing a definition. The normal and customary meaning of "patient" is a person who receives health-related services *from another*. *See* WEBSTER'S NEW WORLD DICTIONARY 990

(3d college ed. 1991). Furthermore, the Court construes the term to give every word meaning, and MRI's interpretation renders "patient" redundant to "human." *See Exxon Chem. Patents*, 64 F.3d at 1557.

Similarly, the Court is not persuaded by BSN that the term requires administration under a physician's direction. There is no indication in the '707 patent that the method was contemplated for use only under a physician's care. However, the Court is persuaded by BSN to the extent that "patient" implies treatment by a qualified health service provider—e.g., physician, nurse practitioner, nutritionist, physical therapist—and therefore construes the term as "the recipient of any of various health service providers."

Administer/administration

The Court agrees with MRI and construes the term as "delivering the formulation-in-question into a person's body." BSN argues that the term should be construed as "giving remedially," but fails offer any support for this interpretation.

Maintaining a therapeutic level of AAKG in the patient's circulatory system

The Court agrees with MRI that this term does not require construction. BSN argues that the term should be construed as "maintaining at least 25 ng/mL of [AAKG] in the patient's circulatory system and in a sufficient level that is sufficient to treat the disease in the patient taking the formulation." As previously discussed, the Court has construed "therapeutic level" and "patient." The remaining words in the phrase—"maintaining" and "circulatory system"—do not require construction.

Therapeutically effective period of time

The Court agrees with MRI that this term does not require construction. BSN argues that the

term should be construed as "greater than four hours." BSN argues that the patentee explicitly excluded any time period less than four hours because the specification stated "[t]he [AAKG] blood plasma level obtained via the present invention is insufficient to obtain a desired therapeutic effect if that level is maintained for only a short period of time, e.g. 4 hours or less." '707 Patent col.6:56-59. Again, BSN improperly attempts to import a claim limitation from the specification. The language BSN cites is merely an example. The specification discusses effectiveness in general terms: "maintaining a minimal [AAKG] blood serum level over time" would treat a patient's symptoms or risk of developing disease.

CONCLUSION

For the foregoing reasons, the Court interprets the claim language in this case in the manner set forth above. For ease of reference, the Court's claim interpretations are set forth in a table as Appendix B. The claims with the disputed terms in bold are set forth in Appendix A.

So ORDERED and SIGNED this 12th day of January, 2007.

LEONARD DAVIS
UNITED STATES DISTRICT JUDGE

APPENDIX A

U.S. PATENT NO. 6,905,707 B2

What is claimed is:

1. A controlled release oral dosage formulation, comprising:

about 50-70% arginine α-ketoglutarate;

and an **excipient material comprising the remainder of the formulation**; **wherein excipient is chosen from microcrystalline cellulose, hydroxypropylmethyl cellulose, ethylcellulose, cellulose acetate butyrate, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyethylene oxide, polyvinylpyrrolidone, polyethylene glycol, zein, poly-DL-lactide-co-glycolide, dicalcium phosphate, calcium sulfate, and mixture thereof**;

wherein the formulation is characterized by releasing the arginine **α-ketoglutarate** in a manner so as to increase a period of time over which a **therapeutic level** of **arginine α-ketoglutarate** is maintained as compared to a quick release formulation**.**

2. The formulation of claim **1**, wherein the releasing is in a manner which maintains the **therapeutic level** of arginine **α- ketoglutarate** for a period of time which is 10% or more longer as compared to a quick release formulation.

3. The formulation of claim **1**, wherein the releasing is in a manner which maintains the **therapeutic level** of arginine **α- ketoglutarate** for a period of time which is 50% or more longer as compared to a quick release formulation.

4. The formulation of claim **1**, wherein the releasing is in a manner which maintains the **therapeutic level** of arginine **α- ketoglutarate** for a period of time which is 100% or more longer as compared to a quick release formulation.

5. The formulation of claim **1**, wherein the releasing is in a manner which maintains the **therapeutic level** of arginine **α- ketoglutarate** for a period of time which is 200% or more longer as compared to a quick release formulation.

6. The formulation of claim **1**, wherein the releasing is sufficiently slow that a maximum level of arginine **α- ketoglutarate** obtained is less as compared to a maximum level obtained with a quick release formulation.

7. The formulation of claim **1**, wherein the releasing is sufficiently slow that a maximum level of arginine **α- ketoglutarate** obtained is 50% or more, less as compared to a maximum level obtained with a quick release formulation.

8. The formulation of claim **1**, wherein the releasing of arginine **α- ketoglutarate** is at a rate of about 25% or less per hour after an initial release rate within 30 minutes following **administration** as compared to a quick release formulation.

9. The formulation of claim **1**, wherein the releasing of arginine **α- ketoglutarate** is at a rate of about 50% or less per hour after an initial release rate within 30 minutes following **administration** as compared to a quick release formulation.

10. A **method of treating atherosclerosis** in a **human patient**, comprising:

administering to a **human patient** a controlled release formulation of **arginine α-ketoglutarate** which formulation is characterized by maintaining a **therapeutic level** of **arginine**

α-ketoglutarate in the patient's circulatory system over a period of time greater than that obtained with a quick release formulation;

and repeating the **administering** on three or more consecutive days thereby maintaining a **therapeutic level** of **arginine α-ketoglutarate in the patient's circulatory system** over a **therapeutically effective period of time** on three or more consecutive days.

11. The method of claim **10**, wherein the **therapeutic level** is maintained over a period of time which is 10% or more than that obtained with a quick release formulation and further wherein the repeating is over thirty or more consecutive days.

12. The method of claim **10**, wherein the **therapeutic level** is maintained over a period of time which is 100% or more than that obtained with a quick release formulation and further wherein the repeating is over thirty or more consecutive days.

13. The method of claim **12**, wherein the **therapeutic level** is a level sufficient to obtain measurable increase in prolyl hydroxylase and lysyl hydroxylase activity in a **human patient**.

14. The method of claim **12**, wherein the **therapeutic level** is a level sufficient to prevent protein glycation associated with **atheroslerosis**, cataract formation and retinopathy.

APPENDIX B

CLAIMS CONSTRUCTION FOR U.S. PATENT NO. 6,905,707

Claim Language	Court's Construction
Arginine α-ketoglutarate Claims 1-10	arginine α-ketoglutarate which is a salt also known as arginine 2-ketoglutarate, arginine 2-oxoglutamate, and arginine 2-oxopentanedioic acid. Unless specified, the term covers racemic mixture as well as any other (non-50/50) mixture of the enantiomers including substantially pure forms of either the R-(+) or the S-(-) enantiomer. Further, unless specified otherwise the term covers pharmaceutically acceptable salts (e.g. Na and K salts) and amides, esters and metabolites of the acid.
Excipient Material Claim 1	any compound forming a part of the formulation which is intended to act merely as a carrier, i.e., not intended to have biological activity itself
About 50-70% Claim 1	no construction needed
an excipient material comprising the remainder of the formulation Claim 1	the formulation includes only AAKG and excipient materials
wherein excipient is chosen from microcrystalline cellulose, hydroxypropylmethyl cellulose, ethylcellulose, cellulose acetate butyrate, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyethylene oxide, polyvinylpyrrolidone, polyethylene glycol, zein, poly-DL-lactide-co-glycolide, dicalcium phosphate, calcium sulfate, and mixture thereof; Claim 1	wherein excipient is chosen from microcrystalline cellulose, hydroxypropylmethyl cellulose, ethylcellulose, cellulose acetate butyrate, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyethylene oxide, polyvinylpyrrolidone, polyethylene glycol, zein, poly-DL-lactide-co-glycolide, dicalcium phosphate, calcium sulfate, and mixtures of two or more of the above listed excipients and may include excipients not listed

Therapeutic Level Claims 1-5, 10-14	a level that is above the baseline level in the body and is sufficient to obtain the desired therapeutic result
Method of Treating Atherosclerosis Claim 10	method of treating: obtaining a desired pharmacological and physiological effect; the effect may be prophylactic in terms of preventing or partially preventing a disease, symptom or condition thereof and/or may be therapeutic in terms of partial or complete cure of a disease, symptom, or adverse effect attributed to the disease
Atherosclerosis Claims 10, 14	a disease, symptom, or condition characterized by a progressive narrowing and hardening of the arteries
Human Patient Claims 10, 13	a recipient of any various personal health services
Administering, Administration Claims 8-10	delivering the formulation-in-question into a person's body
Maintaining a therapeutic level of AAKG in the patient's circulatory system Claim 10	no construction needed
Therapeutically effective period of time Claim 10	no construction needed